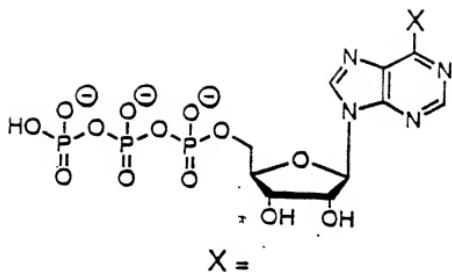


Figure 1



- | | | | | | |
|----|---|----|---|-----|--|
| 1: | $\begin{array}{c} \text{---N---OCH}_3 \\ \\ \text{H} \end{array}$ | 6: | $\begin{array}{c} \text{---NH---O---} \\ \\ \text{Ph} \end{array}$ | 10: | $\begin{array}{c} \text{---N---} \\ \\ \text{Cyclohexyl} \end{array}$ |
| 2: | $\begin{array}{c} \text{---N---OCH}_2\text{CH}_3 \\ \\ \text{H} \end{array}$ | 7: | $\begin{array}{c} \text{---N---} \\ \\ \text{Cyclopentyl} \end{array}$ | 11: | $\begin{array}{c} \text{---N---} \\ \\ \text{Cyclohexyl} \end{array}$ |
| 3: | $\begin{array}{c} \text{---N---COCH}_3 \\ \\ \text{H} \end{array}$ | 8: | $\begin{array}{c} \text{---N---} \\ \\ \text{Cyclohexyl} \end{array}$ | | |
| 4: | $\begin{array}{c} \text{---N---O---} \\ \\ \text{CH}_3 \\ \\ \text{CH}_3 \end{array}$ | 9: | $\begin{array}{c} \text{---NH---O---} \\ \\ \text{Cyclopentyl} \end{array}$ | | |
| 5: | $\begin{array}{c} \text{---N---} \\ \\ \text{H---} \\ \\ \text{Ph} \end{array}$ | | | 12: | $\begin{array}{c} \text{---NH---O---} \\ \\ \text{Cyclohexyl} \end{array}$ |

Figure 2

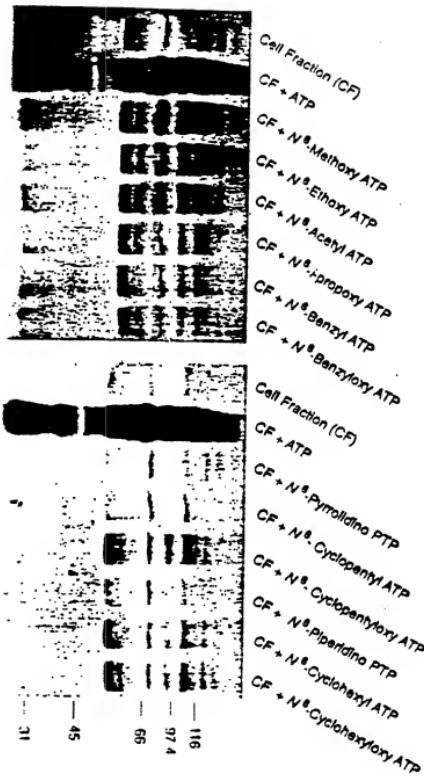


Figure 3

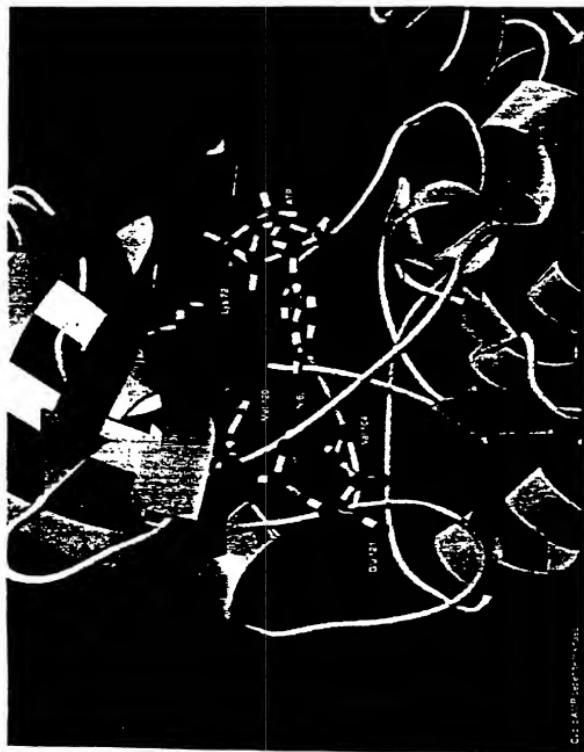


Figure 4

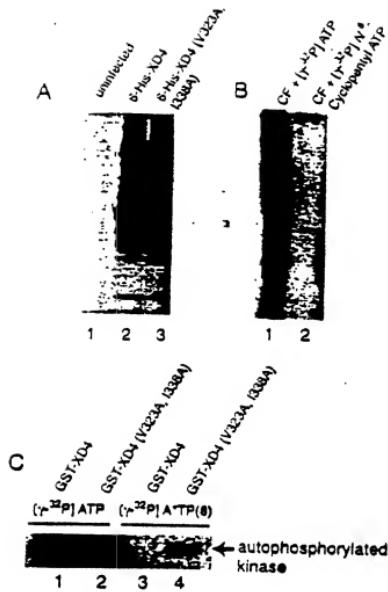


Figure 5

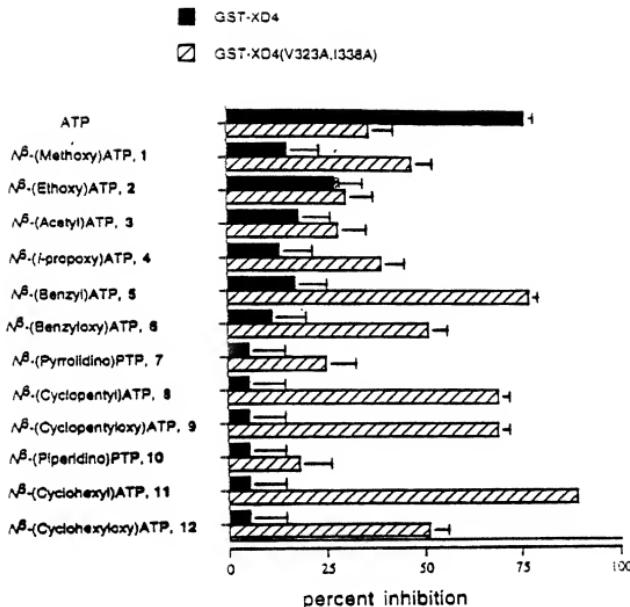


Figure 6

E05470-2964054

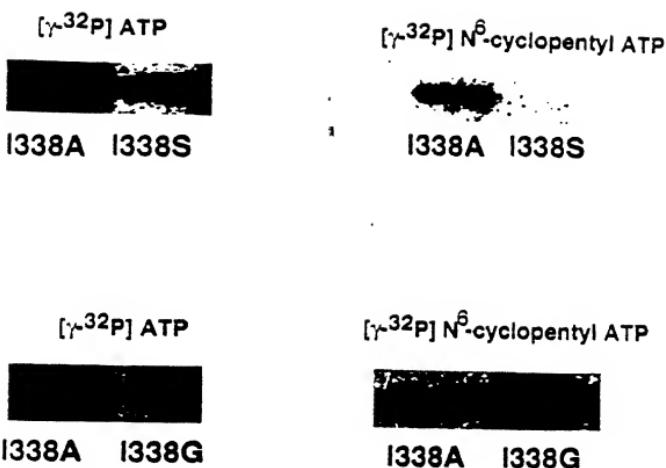


Figure 7

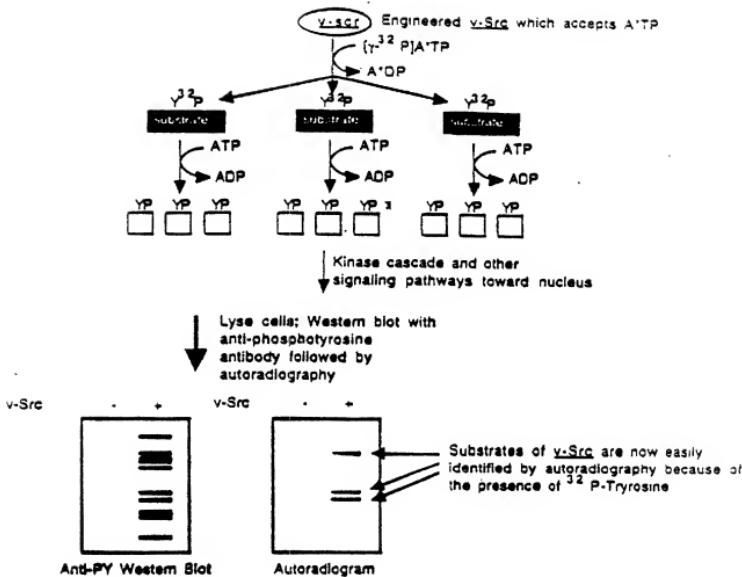
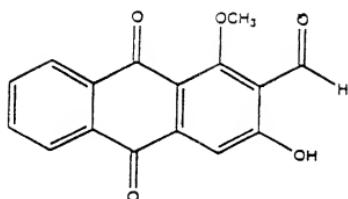


Figure 8

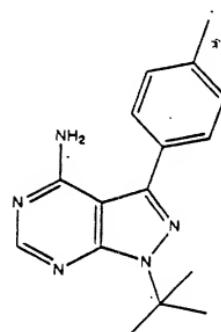
A. Damnnacanthal



IC_{50} (μM)

lck	0.10
fyn	2.09
src	0.68
erbB2	3.5

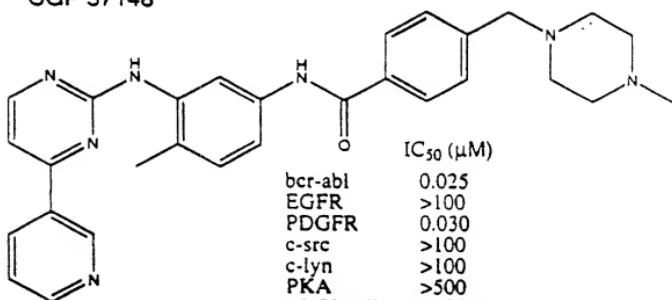
B. PP1



IC_{50} (μM)

lck	0.005
fyn	0.006
src	0.17
hck	0.020
zap-70	>100
JAK2	>50
EGFR	0.25

C. CGP 57148

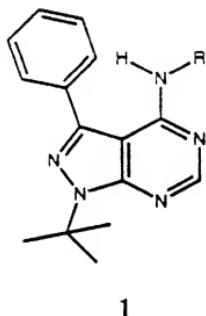


IC_{50} (μM)

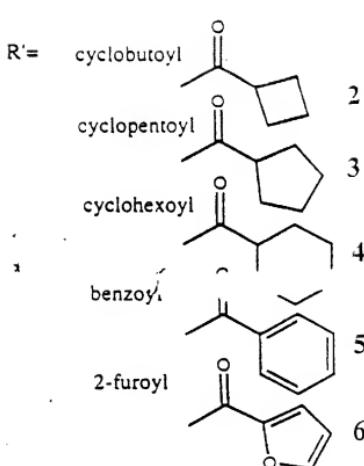
bcr-abl	0.025
EGFR	>100
PDGFR	0.030
c-src	>100
c-lyn	>100
PKA	>500
cdc2/cyclin	>100

Figure 9

A. N-4 Acyl Analogues



B.



C. *In vitro* Inhibition Data

$R' =$	$IC_{50} (\mu M)$		
	WT fyn	WT src	I338G src
H	0.08	35	<1
cyclobutoyl	>>400	>>400	12
cyclopentoyl	400	>>400	5
cyclohexoyl	50	>>400	20
benzoyl	>400	>>400	50
2-furoyl		>>400	150

Figure 10

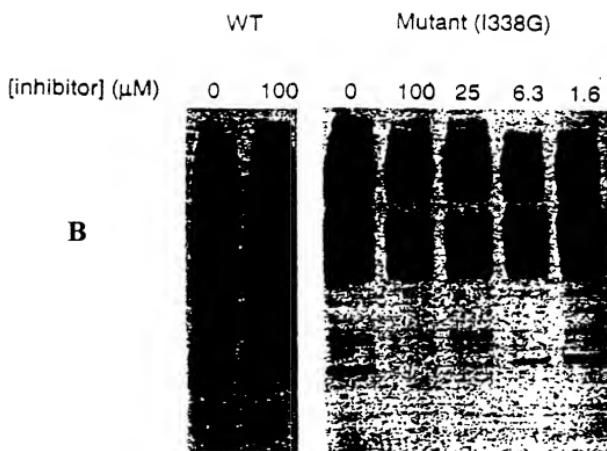
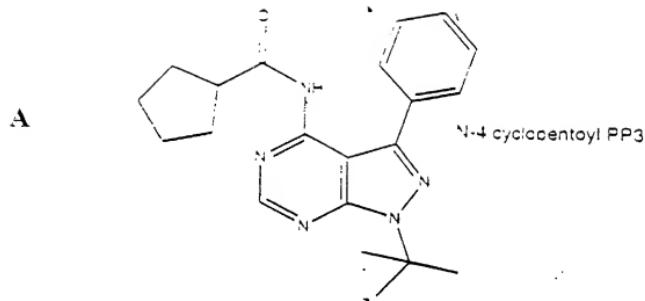


Figure 11

IC₅₀ (μM)

Molecule	WT XD4	T338G XD4	WT Fyn	T339G Fyn	WT Abl	T110A Abl
a		35	0.13	0.05		<<10
b			200	>300		
c			300	>300		
d			>300	>300		
e		>300	75	>300	100	>10
f		>300	250	>300	26	>10
g		>300	85	>300	63	>10
h						
i						

Figure 12A

j							
k							
l		>300	12	6.5	5		
m		>300	19	80	9		
n		>300	20	50	5		
o		>300	150	15	19		
p		>300	10	300	11		(10)
q		>300	10	300	6		(10)
r			1.2				<10
s			0.63				
t			(0.411)				1.8
u		>300	0.43	300	0.83	300	(10)

Figure 12B

10044957-041502

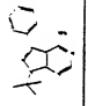
v							
w							
x							>10
y		100	(0.05	0.1			
z			>100	>300			
aa				2			
bb				7			
cc							
dd							
ee							

Figure 12C

ff							
gg							
hh							
ii							
jj							
kk							
ll							
mm							
nn		>1000	0.510	0.4		<<6.5	
oo		>300	>10	>300			

Figure 12D

	>300	>10	>300			
	>300	>10	>300			
	>300	>10	>300			
	>300	>10	>300			
	>300	>10	>300			
	>300	>10	>300			
	>300	>10	>300			
	>300	>10	>300			
	>300	>10	>300			

Figure 12E

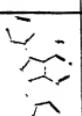
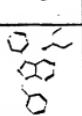
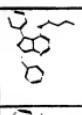
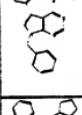
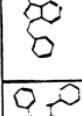
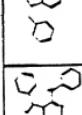
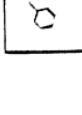
						
	<10	2.5	<<10			
	>300	>10	>300			
	>300	>10	>300			
	>300	>10	>300			
	>300	>10	>300			
	>300	>10	>300			
	>300	>10	>300			

Figure 12F

Figure 13A

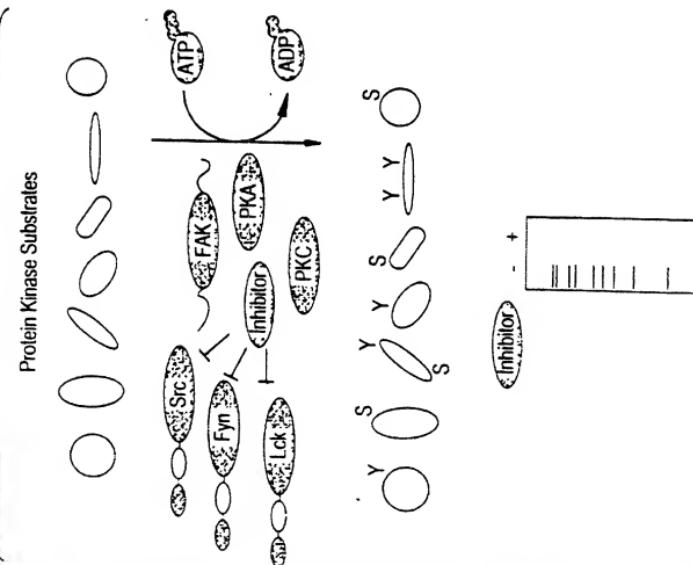
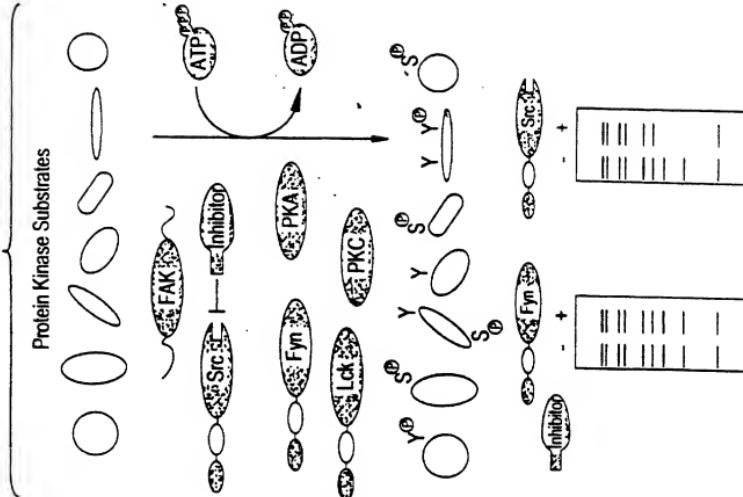


Figure 13B



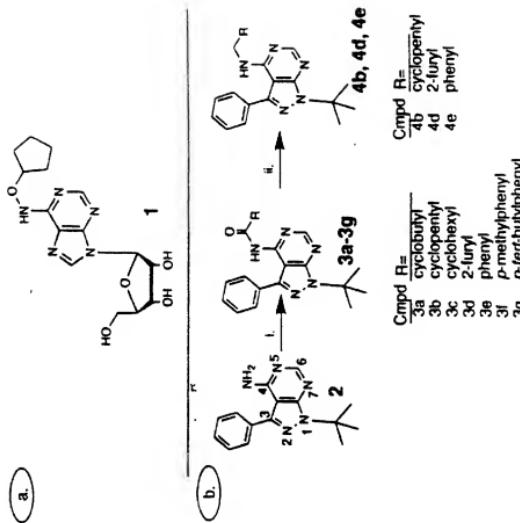


Figure 14

2007-01-15 09:40:11

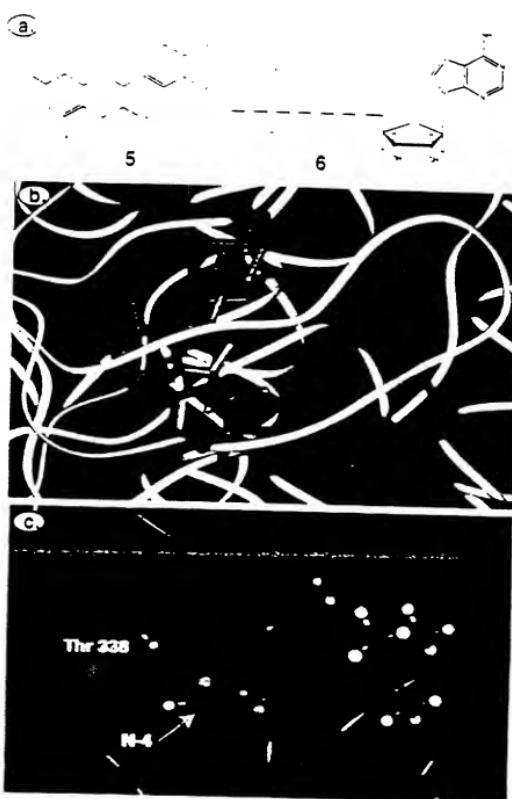


Figure 15

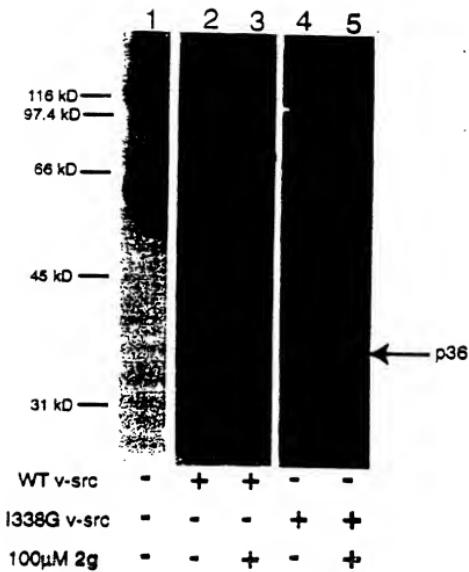


Figure 16

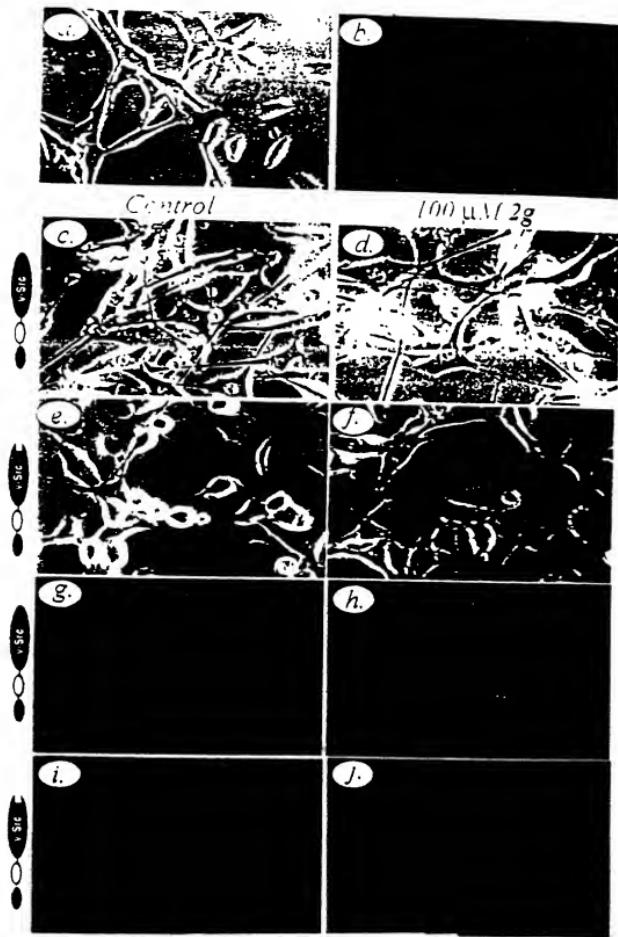


Figure 17

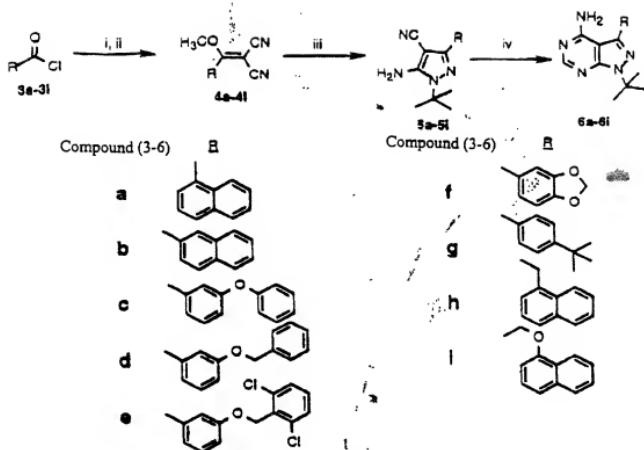


Figure 18

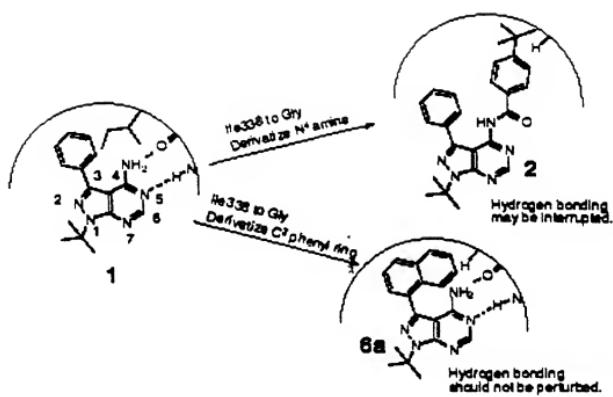


Figure 19

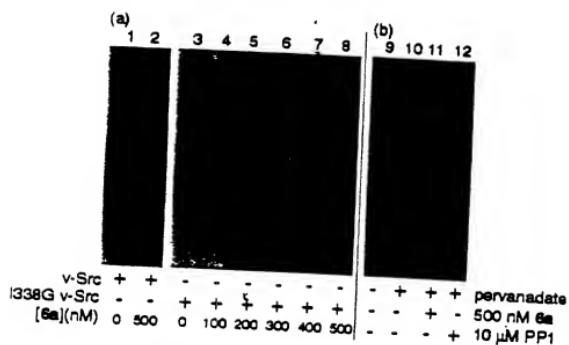


Figure 20

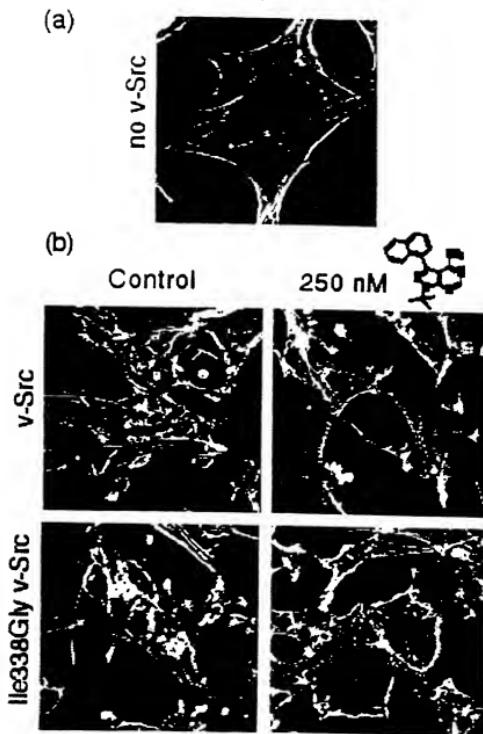


Figure 21

Figure 1

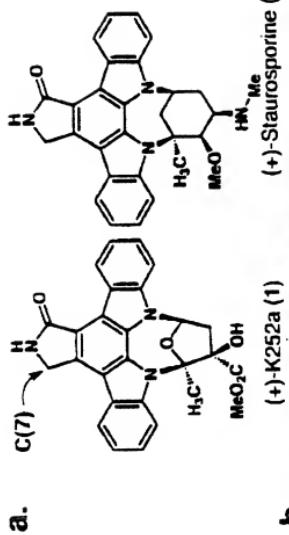


Figure 22



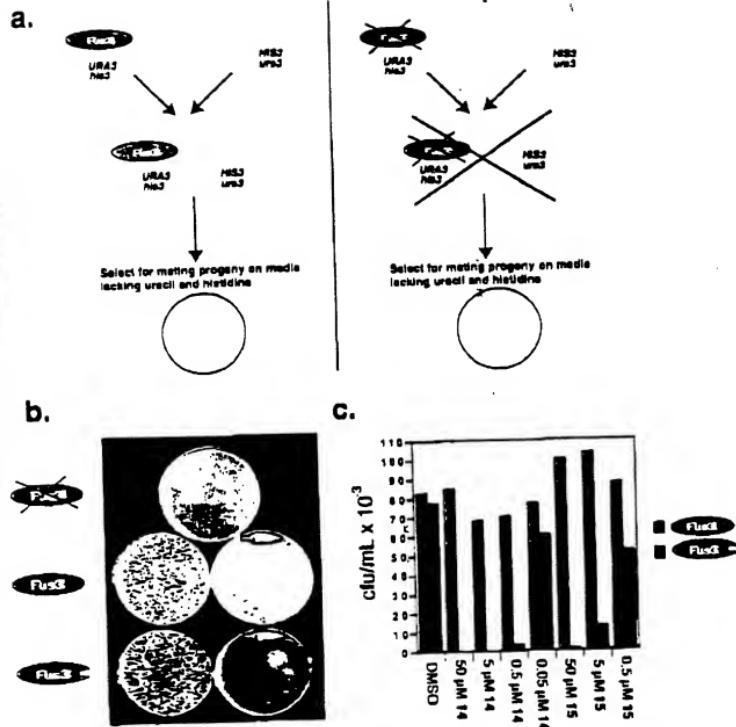
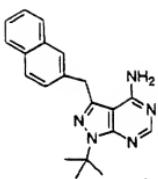


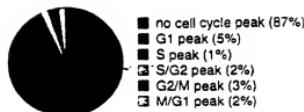
Figure 23



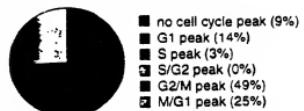
6j

Figure 24

A All *S. cerevisiae* genes (6,200)

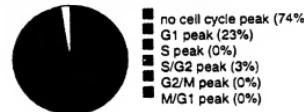


B Decreases - 120 min (66)



	S	S/G2	M/G1
AMT1	-3	HTB2	-1.5
SARI	-5.1	MET14	-2.8
PUT4	-2.2	G2/M	-3.2
SUM1	-2.2	ALK1	-3.5
YBR087C	-3.5	ATP2	-4.1
YER087W	-3.5	SHD1	-3.7
	CDC28	STZ2	-2.8
G1	-6.4	CDCC28	-4.1
CT51	-2.2	CDC28	-3
DRH1	-2.2	CLB2	-4.1
MPA1	-3.2	DRB2	-2.8
PRY2	-2.7	FAR2	-25.4
RAD1	-2.2	HOT2	-4.1
RPC10	-4.2	MPA2	-4.8
SCW11	-16.4	MYO1	-3
TER114C	-4.4	MPD1	-4.8
YHR218W	-3	PNO12	-5.1
		YRQ2	-7.8
G1			IC54
CMS2			-4.7
PCL8			-2.5
PRL1			-3.7
TPF1			-3.5
SPR1			-7.8
TCP1			-5.5
YDR049W			-3.1
YDR067C			-19.4
YDR068W			-1.7
YDR147W			-4.7
YFL158C			-4.6

C Increases - 120 min (38)



	Unreg.	G1	S	S/G2	G2/M	M/G1	S/G2	IC54
BCD	2.8	YAR087W	4.5				3.3	
DNC1	2.8	YBR214C	3.7				3.2	
ERR1	2.8	YCR049C	2.8				4.7	
DRB2	3.2	TEL070W	3				2	
GUT2	2.8	YFL061W	3.2				2.8	
HEM13	2.8	YGL081W	2.2				2.8	
HAL1	2.1	YOL102W	2.2				2.8	
MPD1	2.7	YHR214W-A	2.8				4	
MPR20	2.7	YIL186W	26.1				2.8	
NDR1	2.5	YLR120C	2.7				3.4	
PEXA	2.8	YLR320C	2.1				2	
SKM1	2.7	YMR120C	2.7				2.7	
SPD211	5.8	YMR127W	3.2				3.2	
THB12	2.8	YOR120C	2.3				2.3	
THB21	2.5	YPL38WW	3.1					

D Genomic trends

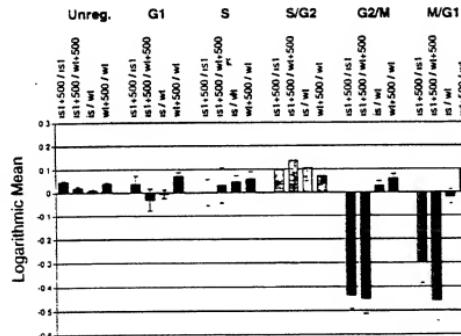
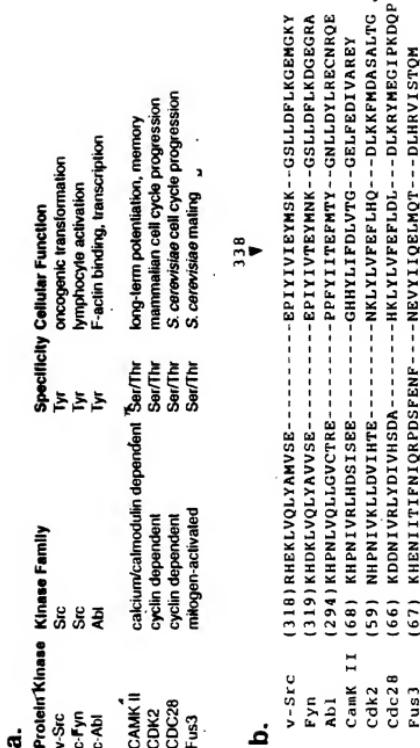


Figure 25

Figure 26



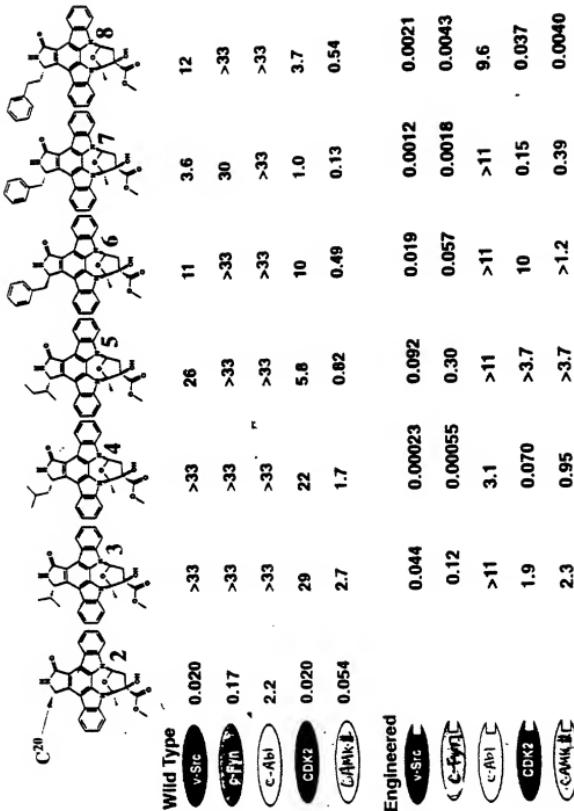
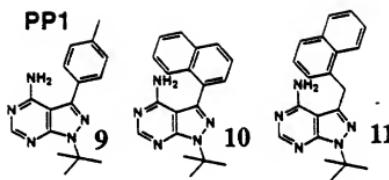


Figure 27

**Wild Type**

v-Src	2.2	1.0	28
c-Fyn	0.050	0.60	1.0
c-Abi	0.30	0.60	3.4
CDK2	22	18	29
CAMK II	17	22	24

Engineered

v-Src	0.0015	0.0043
c-Fyn	0.0065	0.0032
c-Abi	0.0070	0.12
CDK2	0.015	0.0050
CAMK II	0.097	0.0080

Figure 28